

Title: Menopause and Hormone Replacement Therapy in Women with Inflammatory Bowel Diseases in CCFA Partners

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Background: The impact of menopause and cessation of hormonal fluctuation on disease activity in patients with inflammatory bowel disease (IBD) is unknown. IBD diagnosis may also have an impact on the timing and symptoms surrounding onset of menopause. We therefore aimed 1) to assess the characteristics of menopause in women with IBD, 2) to evaluate the impact of menopause (natural and surgical) and hormone replacement therapy (HRT) on disease activity among women enrolled in CCFA Partners.

Method: A subset of female participants in CCFA Partners completed a reproductive health survey including questions on type and onset of menopause (n=2252). We performed cross-sectional analyses a) describing characteristics of menopause in women with IBD and b) comparing various characteristics, including disease activity, in age-matched women with and without menopause. Disease activity was measured via the short Crohn's disease activity index (sCDAI) for Crohn's disease (CD) and simple clinical colitis activity index (SCCAI) for ulcerative colitis/indeterminate colitis (UC/IC). We used bivariate analyses and logistic regression models to investigate associations between disease activity and menopause status, type of menopause, and HRT

Results: A total of 1434 women with CD and 818 with UC/IC were included in the analysis. Menopause was reported in 533 (27.2%) and 266 (32.6%) in CD and UC/IC, respectively. The majority of patients reported natural menopause, 57.2% and 60.8% for CD and UC/IC patients, respectively. The mean age of onset for natural menopause in this cohort was comparable to the general population, 50 (SD=4) in both disease subtypes. Current HRT use was reported in 33.5% and 35.6% of post-menopausal women with CD and UC/IC, respectively. Menopause was associated with increased disease activity in both disease subtypes (OR 1.73, 95% CI 1.19-2.50 in CD and OR 2.93, 95% CI 1.78-4.84 in UC/IC). Within strata of age, menopause status (as compared to age-matched women with no menopause) was associated with active disease (defined as CDAI>150 or SCCAI >2) in women at age \leq 45 (OR 3.07, 95% CI 1.51-6.24 in CD and OR 5.94, 95% CI 1.34-26.37 in UC/IC) but had only borderline association with disease activity in CD patients older than 45 and no association with disease activity in UC/IC patients older than 45. In post-menopausal women, neither type of menopause nor HRT use predicted disease activity in either CD or UC/IC.

Conclusion: Menopause was associated with increased disease activity for patients at age \leq 45 but had no significant impact in older patients. This age variation suggests a different disease process in older patients with a reduced impact of hormonal changes. Interestingly, HRT was not associated with alterations in disease activity in any strata of age within this cohort.

Table 1: Predictors of disease activity within age strata in patients with CD and UC/IC

Variables	CD		UC/IC	
	Age ≤ 45 (n= 807) OR (95% CI)	Age >45 (n= 585) OR (95% CI)	Age ≤ 45 (n= 472) OR (95% CI)	Age >45 (n= 314) OR (95% CI)
Post-menopausal status	3.02 (1.46-6.25)*	1.65 (1.03-2.52)*	6.3 (1.40-28.21)*	1.56 (0.91-2.69)
Current tobacco use	2.96 (1.65-5.29)*	1.74 (0.97-3.13)	N/A	N/A
Current steroid use	3.64 (2.42-5.46)*	2.71 (1.66-4.44)*	4.05 (2.13-7.72)*	2.89 (1.25-6.65)*
Current immunomodulator therapy	0.84 (0.62-1.15)	0.96 (0.66-1.39)	0.82 (0.52-1.29)	1.88 (1.07-3.34)*
Current biologics therapy	1.02 (0.76-1.37)	1.16 (0.81-1.66)	0.97 (0.62-1.53)	1.29 (0.69-2.45)

*Statistically significant value (P <0.05)

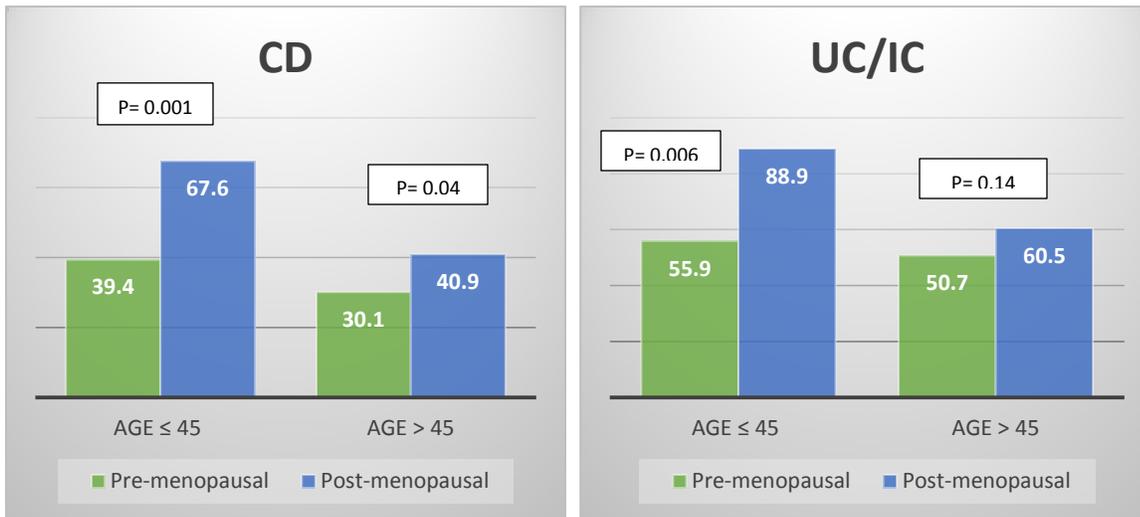


Figure 1: Percentages of patients with active disease (defined as CDAI > 150 or SCCAI > 2) in non-menopausal and post-menopausal women stratified by age and disease subtype